

Amendment to the Specification

At the end of the specification, after the listing of “References,” and before the claims, please insert the following new paragraph:

[00527] In accordance with 37 C.F.R. § 1.52(e)(5), a Sequence Listing in the form of a text file (entitled “Sequence_Listing,” created on June 1, 2009, and 107 kilobytes) is incorporated herein by reference in its entirety.

Beginning on a new page, after the above-referenced new paragraph [00527], and immediately before the claims, please insert the attached Sequence Listing into the above-referenced case; please renumber subsequent pages accordingly. Applicant submits that the instant Amendment includes no new matter.

Please replace paragraph [0037] with the following amended paragraph:

[0037] *Figures 16A and 16B* show schematic diagrams illustrating the differences between influenza virus vRNA, mRNA, and cRNA (template RNA) and the relationships between them. The conserved 12 nucleotides at the 3’ end and 13 nucleotides at the 5’ end of each influenza A virus vRNA segment are indicated in Figure 16B. The mRNAs contain an m⁷GpppN^m cap structure and, on average, 10 to 13 nucleotides derived from a subset of host cell RNAs. Polyadenylation of the mRNAs occurs at a site in the mRNA corresponding to a location 15 to 22 nucleotides (SEQ ID NO: 272) before the 5’ end of the vRNA segment. Arrows indicate the positions of primers specific for each RNA species. (Adapted from ref. (1)).

Please replace paragraph [00351] with the following amended paragraph:

[00351] As described above, during replication of influenza virus, vRNA is transcribed to produce cRNA, which serves as a template for more vRNA synthesis, and mRNA, which serves as a template for protein synthesis (1). Although RNAi is known to target the degradation of mRNA in a sequence-specific manner (16-18), there is a possibility that vRNA and cRNA are also targets for siRNA since vRNA of influenza A virus is sensitive to nuclease (1). To investigate the effect of siRNA on the degradation of various RNA species, reverse transcription using sequence-specific primers followed by real time PCR was used to quantify the levels of vRNA, cRNA and mRNA. Figure 16 shows the relationship between influenza virus vRNA,

mRNA, and cRNA. As shown in Figures 16A and 16B, cRNA is the exact complement of vRNA, but mRNA contains a cap structure at the 5' end plus the additional 10 to 13 nucleotides derived from host cell mRNA, and mRNA contains a polyA sequence at the 3' end, beginning at a site complementary to a site 15 – 22 nucleotides downstream from the 5' end of the vRNA segment. Thus compared to vRNA and cRNA, mRNA lacks 15 to 22 nucleotides at the 3' end. To distinguish among the three viral RNA species, primers specific for vRNA, cRNA and mRNA were used in the first reverse transcription reaction (Figure 16B). For mRNA, poly dT18 (SEQ ID NO: 112) was used as primer. For cRNA, a primer complementary to the 3' end of the RNA that is missing from mRNA was used. For vRNA, the primer can be almost anywhere along the RNA as long as it is complementary to vRNA and not too close to the 5' end. The resulting cDNA transcribed from only one of the RNAs was amplified by real time PCR.